Insidious Mycobacterium tuberculosis infection causing tubulointerstitial nephritis is a rare disorder. Here we report on a single-center case series of patients with tubulointerstitial nephritis due to tuberculosis, addressing clinicopathologic features and treatment outcome. Twenty-five adult patients with clinical evidence of tuberculosis and significant renal disease were assessed, 17 of whom had a kidney biopsy and were subsequently diagnosed with chronic granulomatous tubulointerstitial nephritis as the primary lesion. All patients were given standard antitubercular treatment, with some receiving corticosteroids, and showed a good response in clinical symptoms and inflammatory markers. Nine of the 25 patients, however, started renal replacement therapy within 6 months of presentation. Of the remaining 16, renal function improved for up to a year after presentation but subsequently declined through a median follow-up of 36 months. This case series supports that chronic tubulointerstitial nephritis is the most frequent kidney biopsy finding in patients with renal involvement from tuberculosis. Thus, a kidney biopsy should be considered in the clinical evaluation of kidney dysfunction with tuberculosis since tubulointerstitial nephritis presents late with advanced disease. A low threshold of suspicion in high-risk populations might lead to earlier diagnosis and treatment, preserving renal function and delaying initiation of renal replacement therapy.

Tuberculosis (TB) of the genitourinary tract, like other forms of the disease, is caused by members of the Mycobacterium tuberculosis complex. Globally, it is estimated that 9.2 million new cases and 1.7 million deaths from TB occurred in 2006, of which 0.7 million cases and 0.2 million deaths were in human immunodeficiency virus (HIV)-positive people. Most of the TB infections are in the lung, but extrapulmonary TB accounts for 20–25% of the total worldwide disease burden, and in 12% of cases there is both pulmonary and extrapulmonary TB. The genitourinary system is the second most common site of extrapulmonary TB, affected in 15–20% of nonpulmonary infections, but isolated genitourinary TB is a feature in just 4% of patients. The global incidence of TB per capita peaked around 2003 and appears to have stabilized or begun to decline by 2006, but the incidence of TB in the United Kingdom and particularly in London continues to rise. The incidence of this disease is much higher in ethnic minority populations in the United Kingdom, and has also been found to be higher in patients with chronic renal failure. Although the epidemiology of pulmonary TB in England and Wales and identification of at-risk groups is well defined from previous National surveys, the epidemiology of genitourinary TB is not well described.

TB can cause renal impairment in a variety of ways. TB of the kidneys leading to renal failure is an important, although rare, cause of renal failure as it is potentially treatable. Genitourinary TB has been well described in the form of a ‘classical’ presentation with sterile pyuria, pelvicalyceal deformities, and (usually) systemic symptoms. However, tubulointerstitial nephritis (TIN) due to TB is a more insidious and less well-recognized form of renal involvement in TB, which has previously been described in a small case series from our center. Subsequent case reports have been infrequent and with small patient numbers. There is evidence that subclinical TIN was present in >25% of patients with pulmonary TB in a small biopsy series. However, this is likely to include patients with drug-induced interstitial nephritis, as most of the patients were on treatment with antitubercular agents at the time of biopsy. Tuberculous TIN has been found to be more common in patients from the Indian subcontinent, and has been postulated to be because of a pauci-immune-complex-mediated inflammatory reaction. A single-center series of 394 consecutive
patients undergoing diagnostic renal biopsy in west London has also shown an increased incidence of interstitial nephritis of unknown etiology in the subgroup of patients from the Indian subcontinent, with 15 out of the 19 patients with unexplained interstitial nephritis being of Indian origin.\textsuperscript{12}

The mainstay of treatment in this disease is the standard recommended regimen of antitubercular therapy consisting of 6 months of isoniazid and rifampicin, supplemented in the first 2 months with pyrazinamide and ethambutol.\textsuperscript{13} However, in view of the evidence for irreversible optic neuritis with ethambutol treatment in patients with significant renal impairment,\textsuperscript{14} some renal units have a policy of withholding ethambutol treatment and initiating treatment with three agents followed by standard course of two agents. Our unit has a policy of individualized therapy under the supervision of a nephrologist and a chest physician specializing in TB in such patients. There are no data on steroid therapy in TB TIN and neither the British Thoracic Society/National Institute for Clinical Excellence in the United Kingdom nor the Centre for Disease Control/American Thoracic Society in the United States\textsuperscript{15} specifically recommend steroid therapy in the treatment of TB TIN. However, this is with the caveat that the guidelines are focused on the treatment of classical deforming genitourinary TB rather than TB TIN. The evidence for steroid treatment in idiopathic TIN remains ill defined\textsuperscript{16} in the absence of trial data, which is not surprising in view of the rarity of the condition. Our policy now is to initiate steroid treatment at the dose of 0.5 mg per kg body weight of prednisolone in patients with severe and progressive renal dysfunction and a diagnosis of TB TIN, with tapering of the steroid dose after 2 months of treatment.

There is a paucity of data on the impact of therapy on long-term outcome, the risk of drug toxicity, and progression of chronic kidney disease (CKD) in TB TIN. We present the largest single-center series of TIN due to TB treated with a combination of antitubercular treatment and corticosteroids.

RESULTS

Patients

In all, 25 adult patients were assessed by the renal unit between January 2001 and August 2008 with clinical evidence of TB and significant renal disease. In total, 17 patients (68\%) underwent a renal biopsy. The cohort of 25 patients included 2 patients (8\%) who had HIV co-infection, of whom one underwent a renal biopsy.

The median age at presentation was 40 years (range 20–75 years) with 11 male patients. The median age was 40 years (range 20–75 years) with 11 male patients. Of the 25 patients, 19 were of Indo-Asian ethnic origin and 6 patients were of Black African origin (Table 1). Co-morbidity varied with the country of origin of the patient, with two out of six patients of Black African origin presenting with HIV co-infection and sputum-positive TB; the remaining patients did not have HIV co-infection and presented with more indolent symptoms. The total length of stay in the United Kingdom varied from 6 months to 30 years, with six patients having been here for >20 years; three were born in this country.

Of the eight non-biopsied patients, five had microbiological evidence of TB (Figure 1). Three had presented with \textit{M. tuberculosis} culture-positive sputum, of whom one patient had HIV infection with miliary shadowing on chest X-ray, and an early-morning urine culture (EMU) positive for TB. One patient developed granulomatous uveitis with \textit{M. tuberculosis} culture-positive tuberculous peritonitis after presenting with dialysis-requiring renal failure. One patient had axillary and cervical lymphadenopathy with histological and microbiological evidence of TB on lymph node biopsy. The remaining three non-biopsied patients had pyrexia of unknown origin with systemic symptoms of disease, of whom one had three family members with active TB living in the same house, one had retroperitoneal and mediastinal lymphadenopathy, and one had chest X-ray evidence of old TB. All eight patients not biopsied had small (<8.5 cm) smooth kidneys on imaging by computerized tomography or ultrasound examination. The patient with HIV co-infection had normal-sized (11.5 cm, 12.0 cm bipolar length) kidneys on ultrasonography but was not biopsied as he was EMU positive.

Of the 17 patients who underwent a renal biopsy, all had chronic renal impairment, were treatment-naïve for HIV and TB, and were diagnosed with TIN.

Of these 17 patients, 8 (47\%) were asymptomatic and were biopsied on the basis of active urinary sediments with a rapidly progressive renal failure. Of these eight, five (62.5\%) gave a history of systemic symptoms of unexplained weight loss and fever over the preceding 4 to 12 months. Additionally, three patients (37.5\%) gave a history of urinary frequency and nocturia. Two patients were 31- and 42-year-old males without significant prostatomegaly or residual urine, whereas the third patient was a 35-year-old female with dysuria and urinary frequency. Two patients were asymptomatic at presentation.

Two out of the eight patients with no evidence of TB elsewhere were initially treated empirically with oral steroids.
for granulomatous TIN with progressive renal impairment. Both became acutely unwell over a period of 2 to 3 weeks. The first patient, a 37-year-old female of Indo-Asian origin, developed progressive pulmonary infiltrates with sputum smear-positive pulmonary TB. The second patient was a 39-year-old male, also of Indo-Asian origin, who developed an exudative peritonitis that was culture positive for *M. tuberculosis* and revealed granulomata on omental biopsy.

The remaining nine biopsied patients had evidence of TB elsewhere. Of these, two patients had cavitating sputum smear-positive pulmonary TB and two patients had histological evidence of cervical tuberculous lymphadenitis along with pulmonary involvement (one exudative pleural effusion, one bilateral hilar lymphadenopathy). One patient had inguinal cold abscesses with histological and microbiological evidence of TB from skin biopsies. One (male, 72 years old) patient had caseating granulomata on a prostatic biopsy performed to investigate prostatic symptoms and a high prostate-specific antigen following an initial diagnosis of idiopathic TIN. One patient was diagnosed as having idiopathic TIN on renal biopsy and investigated for hilar and subcarinal lymphadenopathy via an ultrasound-guided transbronchial fine needle aspiration that revealed culture-positive *M. tuberculosis*. One patient had evidence of paraaortic lymphadenopathy and another had bilateral hilar lymphadenopathy on imaging, both of which were not technically possible to biopsy or aspirate.

**Histology**

All the 16 renal biopsies from patients without HIV co-infection revealed an interstitial inflammation with eosinophilia and granulomata (Figure 2), whereas caseating granulomata were found in only 3 out of the 16 (18.7%) biopsies. The biopsy from the single patient with HIV co-infection showed severe TIN with eosinophilia but no
granuloma formation, on a background of HIV-associated focal segmental glomerulosclerosis and a culture-positive EMU sample for *M. tuberculosis*.

None of the renal biopsy cores examined were positive for acid and alcohol fast bacilli by Ziehl–Neelsen staining or culture. Out of 17 biopsy cores examined, just 2 had mesangial IgG deposition, which was thought to be nonspecific IgG trapping on a scarred glomerulus. There was no evidence of immune-complex deposition on electron microscopy.

PCR of the clinicopathological samples has been shown to have a poor sensitivity in paraffin-embedded samples. A retrospective study using PCR-based diagnosis of extrapulmonary TB showed that 31.9% of paraffin-embedded tissue was positive for Mycobacterial species. We therefore selected five patients from our cohort with a clinical, histological, and/or microbiological diagnosis of *M. tuberculosis* and submitted them for reverse hybridization-based line probe assay (LiPA; the INNO-LiPA Rif. TB) at the HPA National Mycobacterium Reference Laboratory, which is based at our parent institute and is a supra-national reference unit for diagnosis and characterization of mycobacterial disease.

The characteristics of the five patients submitted to the LiPA probe were:

Case 1. Chronic granulomatous TIN on renal biopsy, and widespread lymphadenopathy with a transbronchial mediastinal lymph node aspirate culture positive for *M. tuberculosis*.

Case 2. Sputum culture positive for *M. tuberculosis* with TB with heavily scarred kidneys with granulomatous TIN on biopsy.

Case 3. Prostatic biopsy suggestive of TB (caseating granulomata) followed by a native renal biopsy showing chronic granulomatous TIN.

Case 4. Renal biopsy showed TIN, treated with steroids as idiopathic TIN, developed exudative ascites, fully sensitive *M. tuberculosis* cultured from peritoneal fluid.

Case 5. Renal biopsy showed caseating granulomata with good clinical and biochemical response to antitubercular treatment.

However, in spite of careful patient selection to ensure that patients with high clinical probability of mycobacterial DNA in kidneys were included, all five patients were negative for *M. tuberculosis* on PCR. Therefore, not all histology samples were submitted for *M. tuberculosis* PCR via the LiPA probe.

We feel that the poor pick-up rate of mycobacterial DNA by PCR in extrapulmonary samples was worsened in our patients by the fact that the samples were old (average age 4 years) and were negative on Ziehl–Neelsen staining.

**Treatment**

All patients were treated with standard 6 months of antitubercular treatment, with an initial 2 months of induction period of three (occasionally four) drugs including rifampicin, under both a nephrologist and a chest physician. All patients were also started on steroids in the form of prednisolone 20 mg. The prednisolone was then tapered off at 5 mg per week with a view toward completely stopping it at the end of the first 2 months of treatment.

Two patients had to discontinue treatment temporarily because of side effects of anti-TB medication. The patient with abdominal, axillary, and chest wall cold abscesses developed a drug-induced dermatitis whereas the one with coexistent TB prostatitis developed drug-induced hepatitis. Both were managed by stopping all medication and sequential re-introduction of therapy. All patients managed to complete 6 months of antitubercular treatment.

The average calculated estimated glomerular filtration rate (eGFR) as calculated by the MDRD (Modification of Diet in Renal Disease) equation for all patients at presentation was 13.39 ml/min (95% confidence interval 8.02–20.08). Table 2 and Figure 3 summarize changes in eGFR in response to antitubercular treatment.

All patients showed a good clinical response in systemic symptoms to antitubercular treatment, with a median follow-up of 36 months (range 6–72 months). Out of 25 patients, 9 patients started RRT within 6 months of presentation. In the remaining 16 patients, the mean eGFR was 18.1 ± 2.2 ml/min at presentation, 29.8 ± 12.7 ml/min at 6 months (eGFR at presentation vs 6 months, *P* = 0.0168), and 32.74 ± 14.4 ml/min at 1 year (eGFR at presentation vs 1 year = 0.013). There was no relationship between response to treatment and degree of initial proteinuria with significant improvement in eGFR at 1 year.

We then investigated the change in eGFR during follow-up of these patients. After the first year, the change in eGFR was −7.21 ml/min/year for CKD 3 and −7.065 ml/min/year for CKD 4 over a median follow-up of 43 months (range 26–60 months) for CKD 3 and 31 months (range 12–50 months) for CKD 4. The mean proteinuria at presentation for all patients was 0.83 g per 24 h (± 0.18). Erythrocyte sedimentation rate was only available in 19 out of the 25 patients. Although sterile leukocyturia has been thought to be common in renal TB, just 13 of the 23 (56.5%) patients had sterile leukocyturia in our series.

For patients who did not require dialysis by the end of first year, mean proteinuria at presentation was 1.47 ± 0.13 g per 24 h and for CKD 4 patients was 1.312 ± 0.55 g per 24 h with preserved serum albumin.

The mean proteinuria at presentation for all patients was 1.31 ± 0.83 g per 24 h (*n* = 25) that decreased to 0.25 ± 0.18 (*n* = 16) by the end of 6 months of treatment (*P* = 0.4819). For patients who did not require dialysis by the end of first year, mean proteinuria at presentation was 1.47 ± 0.13 g per 24 h (*n* = 16) that decreased to 0.93 ± 0.24 g per 24 h (*n* = 16) by the end of 6 months (*P* = 0.0404).

The mean C-reactive protein at presentation for all patients was 36.79 ± 10.45 (*n* = 25) that decreased to 7.652 ± 1.202 (*n* = 25; *P* = 0.0094) at 6 months. Erythrocyte sedimentation rate was only available in 19 out of the 25 patients. The mean erythrocyte sedimentation rate at presentation was 54.32 ± 8.478 cm/h (*n* = 19) that decreased to 29.62 ± 4.450 (*n* = 19) at 6 months (*P* = 0.0313).

Interestingly, urine microscopy and culture results were available in 23 out of 25 patients. Although sterile leukocyturia has been thought to be common in renal TB, just 13 of the 23 (56.5%) patients had sterile leukocyturia in our series.
DISCUSSION

Although rare, TB TIN is a disease with poor renal prognosis. Diagnosis is limited by insidious symptoms and advanced disease at the time of presentation. Early diagnosis and treatment was linked to significant recovery of function in our small cohort of patients.

Alternative causes such as renal sarcoidosis and drugs (for example, antibiotics, nonsteroidal anti-inflammatory agents) must also be excluded from the differential diagnosis of granulomatous TIN. Renal sarcoidosis has been described in a case series from our center. Renal manifestations in sarcoidosis include granulomatous TIN that is infrequently associated with ceseation or asteroid bodies, in a majority of patients, with a minority presenting with other glomerular lesions. All patients with renal sarcoidosis had systemic evidence of the disease, with good response to systemic corticosteroid treatment irrespective of the degree of tubulointerstitial scarring, and were maintained on low-dose steroid therapy with significant improvement in eGFR. In contrast, all patients in the current series showed excellent response in response to antitubercular therapy in systemic symptoms and inflammatory markers.

In our group of patients, 19 patients were of Indo-Asian origin (Table 1), of whom three were born in the United Kingdom and three in Kenya, with 13 patients having been born in the Indian subcontinent. This population cross-section is in keeping with previous experience of TB TIN, which has been reported mainly in Indo-Asian ethnic groups. In our series, three patients with TB TIN without HIV infection

![Table 2 | Patient data](image)

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/gender</th>
<th>Follow-up (mo)</th>
<th>Presenting eGFR</th>
<th>Treatment</th>
<th>Outcome/last eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>41/M</td>
<td>6</td>
<td>10.9</td>
<td>2HRZE+4HR</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>35/F</td>
<td>60</td>
<td>10.65</td>
<td>2HRZ+4HR+</td>
<td>Lost to F/U</td>
</tr>
<tr>
<td>3.</td>
<td>34/F</td>
<td>24</td>
<td>13.3</td>
<td>2HRZE+4HR</td>
<td>HDx at year 4, Tx at year 5</td>
</tr>
<tr>
<td>4.</td>
<td>51/F</td>
<td>36</td>
<td>10.1</td>
<td>2HRZE+4HR</td>
<td>51.37</td>
</tr>
<tr>
<td>5.</td>
<td>38/F</td>
<td>48</td>
<td>4.66</td>
<td>2HRZE+4HR</td>
<td>9.8</td>
</tr>
<tr>
<td>6.</td>
<td>74/M</td>
<td>50</td>
<td>10.9</td>
<td>2HRZ+4HR+</td>
<td>Started HDx at 22 mo</td>
</tr>
<tr>
<td>7.</td>
<td>73/F</td>
<td>58</td>
<td>18.5</td>
<td>2HRZ+4HR+</td>
<td>Started HDx at 54 mo</td>
</tr>
<tr>
<td>8.</td>
<td>45/F</td>
<td>24</td>
<td>42.77</td>
<td>2HRZE+4HR</td>
<td>62.08</td>
</tr>
<tr>
<td>9.</td>
<td>20/M</td>
<td>26</td>
<td>3.98</td>
<td>2RZE+4R, Mexb</td>
<td>HDx immediately</td>
</tr>
<tr>
<td>10.</td>
<td>23/M</td>
<td>21</td>
<td>1.59</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately, Tx at 18 mo</td>
</tr>
<tr>
<td>11.</td>
<td>51/M</td>
<td>23</td>
<td>4.32</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately</td>
</tr>
<tr>
<td>12.</td>
<td>39/M</td>
<td>12</td>
<td>4.1</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately</td>
</tr>
<tr>
<td>13.</td>
<td>37/F</td>
<td>50</td>
<td>4.3</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately, Tx at 46 mo</td>
</tr>
<tr>
<td>14.</td>
<td>58/F</td>
<td>68</td>
<td>5.83</td>
<td>2HRZ+4HR+</td>
<td>PD immediately, HDx at 32 mo</td>
</tr>
<tr>
<td>15.</td>
<td>56/M</td>
<td>48</td>
<td>9.8</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately</td>
</tr>
<tr>
<td>16.</td>
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<td>5.84</td>
<td>2HRZ+4HR+</td>
<td>PD immediately, Tx at 26 mo</td>
</tr>
<tr>
<td>17.</td>
<td>56/F</td>
<td>6</td>
<td>13.1</td>
<td>2HRZ+4HR+</td>
<td>16.55</td>
</tr>
<tr>
<td>18.</td>
<td>54/F</td>
<td>12</td>
<td>15.5</td>
<td>2HRZ+4HR+</td>
<td>21.9</td>
</tr>
<tr>
<td>19.</td>
<td>40/F</td>
<td>18</td>
<td>12.1</td>
<td>2HRZ+4HR+</td>
<td>9.8</td>
</tr>
<tr>
<td>20.</td>
<td>71/M</td>
<td>50</td>
<td>16.5</td>
<td>2HRZ+4HR+</td>
<td>12.5</td>
</tr>
<tr>
<td>21.</td>
<td>39/M</td>
<td>36</td>
<td>66</td>
<td>2HRZ+4HR+</td>
<td>40</td>
</tr>
<tr>
<td>22.</td>
<td>29/F</td>
<td>26</td>
<td>27.8</td>
<td>2HRZ+4HR+</td>
<td>90.8</td>
</tr>
<tr>
<td>23.</td>
<td>26/F</td>
<td>13</td>
<td>12.42</td>
<td>2HRZ+4HR+</td>
<td>21.67</td>
</tr>
<tr>
<td>24.</td>
<td>61/F</td>
<td>12</td>
<td>5.9</td>
<td>2HRZ+4HR+</td>
<td>49.11</td>
</tr>
<tr>
<td>25.</td>
<td>38/F</td>
<td>22</td>
<td>5.37</td>
<td>2HRZ+4HR+</td>
<td>HDx immediately</td>
</tr>
</tbody>
</table>

Abbreviations: E, ethambutol; eGFR, estimated glomerular filtration rate in ml/min; F/U, follow-up; H, isoniazid; HDx, hemodialysis; mo, month; PD, peritoneal dialysis; R, rifampicin; Tx, transplantation; Z, pyrazinamide.

Numbers denote treatment duration in months.
bH-resistant organism isolated from sputum, given moxifloxacin (Mox) 400 mg OD.

![Figure 3 | Response to anti-tubercular treatment: individual estimated glomerular filtration rates (eGFRs) at presentation, completion of treatment (6 months), and 1 year (censored for patients who started renal replacement therapy within 1 year).](image)
It is noteworthy that only 10 out of the 25 (40%) were known glomerular atrophy associated with the previous disease. We feel this could have been because of tubular and function started deteriorating after 2 years post-treatment. Their renal function up to 2 years after the initiation of with an MDRD eGFR of 12 months of presentation. Those patients who presented with an eGFR of >15 ml/min and with less interstitial fibrosis and glomerular atrophy. There is some evidence of over-representation of idiopathic TIN in the Indian population in the United Kingdom compared with other ethnic groups in a previous series from London. It is not clear in that report whether the patients treated with oral steroids (with isoniazid prophylaxis) were those with granulomata TIN; none of these patients were reported to have been treated for TB or reactivated TB during follow-up. Two patients in our series who were treated with systemic corticosteroids became systemically unwell (despite isoniazid prophylaxis), developed disseminated TB, and went on to receive antitubercular treatment, suggesting that treatment with steroids alone is not without risks. Out of the 17 patients who presented with an MDRD eGFR of <15 ml/min, 11 patients had a poor renal outcome and progressed to renal replacement therapy within 12 months of presentation. Those patients who presented with an MDRD eGFR of >15 ml/min showed stabilization of their renal function up to 2 years after the initiation of treatment with antitubercular treatment. However, their renal function started deteriorating after 2 years post-treatment. We feel this could have been because of tubular and glomerular atrophy associated with the previous disease. It is noteworthy that only 10 out of the 25 (40%) were known to medical services in the United Kingdom for >6 months before diagnosis, and 9 (36%) presented with end-stage chemistry or near end-stage chemistry, requiring dialysis within 6 months of presentation. This series demonstrates that TB TIN often presents late with advanced disease. A low threshold of suspicion in high-risk populations might lead to earlier diagnosis; early diagnosis and treatment can preserve renal function and delay initiation of renal replacement therapy. Treatment is important in this group as it can influence patient morbidity and mortality because of TB as well as renal replacement therapy. The optimal duration of antitubercular treatment and the role of corticosteroid treatment in this condition require further investigation.

**MATERIALS AND METHODS**

**Identification of cases and definitions**

We identified 25 patients referred to the Barts and the Royal London Hospital Renal unit during the period January 2001 to August 2007 with TB and renal disease. The indications for renal biopsy were unexplained progressive renal impairment and proteinuric renal disease with or without a previous history of TB. Contraindications were small kidneys on renal imaging or a single-functioning kidney. In 17 patients, a native renal biopsy was indicated and technically possible; all showed TIN. The breakdown of the whole cohort is in Figure 1. The patients with TIN were analyzed with respect to epidemiological and clinical features, including response to therapy with anti-TB treatment and corticosteroids, and length of follow-up. The eGFR was calculated by the four-variable MDRD equation.

**Histological analysis**

Renal biopsy samples were processed in the routine manner and embedded in paraffin wax. The sections were stained with hematoxylin and eosin and Ziehl–Neelsen staining. All of the specimens were reported by two observers and discussed in a clinicopathological conference, with the changes within glomeruli, tubules, interstitium, and vessels documented. These included tubulitis, interstitial inflammation, scarring, and the presence or absence of granulomas, and/or acid and alcohol fast bacilli. Granulomatous TIN was defined as interstitial nephritis in which the inflammatory infiltrate included one or more aggregates of epithelioid cells, with or without ceseation and with or without multinucleate giant cells.

**Statistics**

GraphPad Prism version 5.00 for Windows XP (GraphPad Software, San Diego, CA) was used for the analysis. Paired t-test was used to compare year 0, month 6, year 1, and last documented eGFR in different groups, whereas Student's t-test was used to compare change in proteinuria before and after treatment. A P-value of <0.05 was considered significant. Spearman's rank coefficient was used to correlate renal function with proteinuria.

**DISCLOSURE**

All the authors declared no competing interests.

**REFERENCES**


